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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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[REDACTED] EXAMINER

WESSENDORF, TERESA D

[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1639

DATE MAILED: 07/01/2003

10

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|-----------------------------|------------------------|---------------------|
| Offic Action Summary | Application N . | Applicant(s) |
| | 09/904,248 | HONG ET AL. |
| | Examiner | Art Unit |

-- The MAILING DATE of this communication appears in the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 15 April 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 21-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 21-26 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . | 6) <input type="checkbox"/> Other: _____ . |

Art Unit: 1639

DETAILED ACTION

Status of Claims

Claims 1-20 have been canceled in the Amendment of 12/6/02.

Claims 21-26 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The as-filed specification fails to provide a description for the newly added claim "a plurality of modified mononucleosides." The original disclosure at e.g., page 5 defines the term "nucleoside library" as a plurality of chemically distinct nucleosides. Other than this definition of a library, there is nothing in the disclosure that describes that

Art Unit: 1639

the library is a plurality of modified mononucleosides. It does not recite the different mononucleosides that have been modified. Nor does it describe the kind of modifications in the mononucleosides or the number of different combinations of different modifications that is encompassed by the term plural. Furthermore, the term "plural" is redundant since this is a definition attributed to library. [Reciting where support in the specification the newly presented claim can be found would obviate this rejection].

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons advanced in the last Office action.

Response to Arguments

Applicants argue that the term providing as defined by Webster dictionary mean "to supply or make available" which will be readily understood by a person of ordinary skill in the art. It is further argued that USPTO has historically recognized the term in a method claim as being clear and concise. U.S. Patent Nos. 5,907036 and 5,723,589 is argued to reflect this term. In reply, the specification does not recite how the library is supplied or made available. It is not clear whether the library is supplied by a commercial supplier and made available to the public, as to the present inventors. The specification does not seem to recite the supplier of this library. As regards to the two U.S. Patents reflecting said term, each case is determined on its own facts.

Newly amended claim 21 is rejected under this statute as follows:

1. Claim 21 is unclear whether the first and second nucleosides recited in the providing step are not mononucleosides. Neither the specification nor the claims set forth the differentiating characteristics of each of the nucleosides from the mononucleosides. The metes and bounds of

Art Unit: 1639

the term "plurality of modified nucleosides" are not clearly set forth in the claims or specification.

2. Claim 25 is unclear as to whether the reaction with the third and fourth reagent produces or not a mononucleoside. This is at odds with the base claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 21-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carver (99/64378) in view of Gravert et al (Chemical Reviews, Ref. J) for reasons set forth in the last Office action.

Response to Arguments

Applicants admit that Carver at page 11, lines 13 et seq teaches that a monomer unit is covalently linked to an adjoining unit to prepare a combinatorial library. But argue that Carver merely **mentions** that solid phase and solution phage chemistries

Art Unit: 1639

may be used to synthesize a combinatorial library of the invention. In considering disclosure of a reference, it is proper to take into account not only specific teachings of the reference but also **inferences** which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 159 USPQ 342; *In re DeLise* 160 USPQ 806. The suggested teachings of Carver of using solid phase synthesis to make a library of nucleoside would suffice the finding of obviousness.

Applicants admit that Carver suggest the use of solid phase chemistry but lacks enablement from various perspectives. Among other concern, there is no teaching in the Carver reference which portion of the nucleosides would be coupled to the solid phase. It is further argued that in view of the nucleophilic character of the second reagent, and absent further description of what protecting groups, conditions and type of solid phase coupling is employed, Carvers' suggestion lacks any expectation of success. In reply, applicants' arguments are not commensurate in scope with the claims. None of the claims recite e.g., the use of protecting groups, conditions and type of solid support. Nevertheless, determination of these factors is within the ordinary skill in the art. As stated in the last Office action, solid synthesis of compounds, either a monomer or polymer has advanced markedly that it is now automated. The use of different

Art Unit: 1639

reagents, protecting groups, solid phase are all within the ordinary skill in the art to determine. This is recognized by applicants at e.g., page 6, line 15-30. Applicants state that ".....exemplary suitable reaction protocols and procedures for protection and deprotection of the hydroxy groups in the sugar portion of contemplated nucleosides are well known in the art and are described in Protective Groups in Organic Synthesis....."

Further at page 12, lines 6-21 applicants state that ".....with respect to the solid phase it is contemplated that suitable solid phases may be of any appropriate shape, size and composition . For example, preferred support include Merrifield resin....."

Applicants admit that Gravert teaches synthesis of an oligonucleotide on a soluble polymer wherein hexmethylphosphoramide is employed as a coupling agent between a first and a second nucleoside. But argue that Gravert teaches against the subject matter as presently claimed. In reply, Gravert, as recognized by applicants, uses the specific reagent to couple a first and second nucleoside, not oligonucleotide. Thus, the teachings of Gravert that the hexamethylphosphoamide is conventionally employed to couple two mononucleosides would have led one having ordinary skill to use this known coupling reagent to couple two mononucleosides. The test for combining

Art Unit: 1639

references is not what the individual references themselves suggest but rather what the combination of the disclosures taken as a whole would suggest to one of ordinary skill in the art. In re McLaughlin, 170 USPQ 209 CCPA 1971. The court must approach the issue of patentability in terms of what would have been obvious to one of ordinary skill in the art at the time the invention was made in view of the sum of all the relevant teachings in the art, not in view of the first one and then another of the isolated teachings in the art. In re Kuderna, 165 USPQ 575 CCPA 1970.

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will

Art Unit: 1639

expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T.D. M
T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
6/26/03